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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
10/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/839,946	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-53,60 and 61* is/are rejected.

7)☒ Claim(s) *54-59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/8/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final rejection

1. Amendment and response to Non-Final Office Action filed 8/11/2009 is acknowledged.

2. Claims 50-61 are pending and under consideration.

3. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn. The reasons are discussed following the rejection(s).

4. Applicants' arguments regarding rejection of claims 50-61 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter – have been found to be persuasive. Accordingly, the rejection is withdrawn.

5. ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50-53 & 60-61 are rejected under 35 U.S.C. 102(b) as anticipated by Lee et al. [Science 239, 1288-1291 (1988), IDS, previously cited].

Lee et al. (1988) teach the recombinant production of full length amino acid sequence of porcine Urate oxidase (uricase) which is tetrameric and is substantially pure. Mammalian uricase is disclosed as a tetramer with subunit size of 32,000 Daltons (page 1288, column 2, first paragraph after the abstract). The reference further teaches purification to **homogeneity** of Porcine and murine urate oxidase (see, page 1289, second column). Oxidation of uric acid to allantoin is catalyzed by urate oxidase (see abstract). Increased uric acid level, due to lack of this enzyme in man can lead to gouty arthritis (page 1288, column 2). Further, the mammalian uricase of the prior art and the one instantly would therefore be considered the same no matter whether they were isolated from the natural source or were produced recombinantly (claim 52) and that the

amino acid sequence (claim 53) being the inherent property of the enzyme would therefore be not patentably distinct.

Claim 50 is directed to 'an isolated tetrameric mammalian uricase, wherein said uricase is in a substantially tetrameric form , and wherein less than 10% of said uricase is in a non-tetrameric aggregated form. Claim 51 depends on claim 50, and the added limitation "wherein the uricase is porcine liver, bovine liver or ovine liver uricase". Claim 52 depends on claim 50, and the added limitation "wherein the uricase is recombinant". Claim 53 depends on claim 52, and the added limitation "wherein the uricase has the sequence of porcine, bovine, ovine or baboon liver uricase". Claim 60 depends on claim 50 and the added limitation ' wherein less than 5% of said uricase is in a non-tetrameric aggregated'. Claim 61 depends on claim 60 and the added limitation ' wherein less than 2% of said uricase is in a non-tetrameric aggregated'.

Claim 50 uses the term "substantially" in defining how much uricase must be in tetrameric form in order to be encompassed within the scope of the claim, and wherein less than 10%, 5% or 2% of said uricase is in non-tetrameric form. An analysis of the instant Specification to determine whether Appellants have acted as their own lexicographer in defining "substantially." See Merck & Co., v. *TEVA* Pharmaceuticals USA, Inc., 395 F.3d 1364, 1369-70, 73 USPQ2d 1641, 1646 (Fed. Cir. 2005). The review of the Specification, however, does not reveal that " substantially " has been defined in a way different from its ordinary meaning. We thus interpret " substantially " consistent with its ordinary meaning of '*to a great extent or degree'*. We thus interpret the phrase "wherein said uricase is in a substantially tetrameric form" as encompassing a range of uricase or perhaps a greater extent or degree in tetrameric form, with no limit to the range in general and especially with no upper limit" and thus any prior art uricase preparation that contains such an undefined range of the uricase in tetrameric form is encompassed by claim 50. Less than 10%, 5% or 2% of said uricase is in non-tetrameric aggregated form is interpreted to mean - that 0-10% of said uricase could also be non-tetrameric aggregated.

Lee teaches that porcine liver urate oxidase was obtained commercially and purified to homogeneity, citing footnote 8 (Lee, p. 1289). Footnote 8 states that porcine

liver oxidase was obtained from Sigma, and that murine urate oxidase was purified to homogeneity using the method of Conley (1979). Conley (1979) teaches purification of uricase from mammalian tissue by precipitation under certain dialysis conditions (Conley, abstract).

Appellants assert that the Declaration of Merry R. Sherman, Ph.D, filed under 37 CFR § 1.132 and attached as Exhibit D to the Brief, supports their conclusion that "the authors of Lee would not be expected to have produced an uricase preparation in which at least about 90% of the uricase was in a tetrameric form; instead, more than 10% of the uricase would have been present in a non-tetrameric aggregated form." (Br. 12-13 (emphasis in original).) Dr. Sherman at paragraph 5 of the Declaration, referencing the Specification at page 16, lines 5-8, states that "while mammalian uricases *in vivo* (i. e., associated with the peroxisome) exist as a tetramer, isolated purified preparations of natural and recombinant uricase, as indicated in the present specification and as disclosed by Lee, usually contain a mixture of aggregated non-tetrameric forms of the enzyme, in addition to the tetrameric form."

Page 16, lines 5-8 of the Specification, states:

Purified preparations of naturally occurring and recombinant uricases usually contain a mixture of aggregates of the enzyme, in addition to the tetrameric (140 kDa) form. The percentage of each uricase preparation that is in the tetrameric form generally varies from approximately 20% to 90%.

The Specification, as referenced by the Declaration of Dr. Sherman, thus states that uricase preparations containing up to 90% of uricase in the tetrameric form were **known in the prior art**. Moreover, as discussed above, claim 50 encompasses uricase preparations containing only approximately 90% of the uricase in tetrameric form.

The claims as amended recites “said uricase to be substantially in tetrameric form" which includes a range of tetrameric uricase(s) and especially with no limit to the range in general and with no upper limit,–falls within the purification to **homogeneity** of Porcine and murine urate oxidase achieved by teachings of Lee et al.

The uricase preparations of claims 50-53 is encompassed by the uricase preparation of Lee et al., and is thus anticipated by the reference of Lee et al.

The reference therefore anticipates the claims.

6. Arguments in the BPAI decision (previously presented):

As per the BPAI decision, affirming Examiner (See page 2 of the decision). The BPAI decision on page 3, paragraph 3 – states: "It is axiomatic that in order for a prior art reference to anticipate the claimed invention, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). We find that Lee, when read in light of Appellants' statement of the state of the prior art as set forth in the Specification, anticipates the claimed subject matter of claim 50. Because our reasoning differs from that of the Examiner, and Appellants have not had a fair opportunity to respond to the rejection, we designate our affirmance as a new ground of rejection. *See In re Kronig*, 539 F.2d 1300, 1302-03, 190 USPQ 425,426-27 (CCPA 1976).

The BPAI decision (page 5, paragraph 3 & 4) citing -

Page 16, lines 5-8 of the Specification, states:

Purified preparations of naturally occurring and recombinant uricases usually contain a mixture of aggregates of the enzyme, in addition to the tetrameric (140 kDa) form. The percentage of each uricase preparation that is in the tetrameric form generally varies from approximately 20% to 90%.

The Specification, as referenced by the Declaration of Dr. Sherman, thus states that uricase preparations containing up to 90% of uricase in the tetrameric form were known in the prior art. Moreover, as discussed above, claim 50 encompasses uricase preparations containing only approximately 90% of the uricase in tetrameric form. Therefore, claim 50 encompasses uricase preparations as prepared in the prior art, such as by Lee, and is thus anticipated by the prior art.

CONCLUSION

In summary, we affirm the rejection of claims 50-53 as being anticipated by Lee. Because our reasoning differs from that of the Examiner, we designate the rejection as to those claims as new grounds of rejection.

7. New arguments:

In traversing the rejection of claims 50-53 under 35 U.S.C. 102(b), Applicants argue that "…..claim 50 is directed to "an isolated tetrameric mammalian uricase, wherein said uricase is in a substantially tetrameric form, and wherein less than 10% of said uricase is in a non-tetrameric aggregated form." Thus, by definition the presently claimed tetrameric uricase preparations must contain greater than 90% of the uricase in the tetrameric form.

Applicants' arguments are considered but not found to be persuasive because there is reason to equate "substantially tetrameric form" to mean "greater than 90% of the uricase in the tetrameric form". The specification does not define the word 'substantially' to mean that "tetrameric uricase preparations must contain greater than 90% of the uricase in the tetrameric form; and the dictionary meaning does not support such a conclusion either."

Further, Applicants have repeated argued that the preparations of uricase obtained by Lee for use in the preparative or analytical SDS-PAGE disclosed in that reference are not in the native tetrameric form.

Explaining this issue once again SDS-PAGE separation is a *denaturing* gel separation, i.e. the 'native tetrameric form' when run (or loaded) on to an SDS-PAGE gel is denatured and the tetrameric form of the native uricase is revealed. Therefore, the SDS-PAGE separation technique is merely a technique to reveal or study the property of the protein to identify number of subunits in a purified protein or identify whether a protein is a 'monomer', dimmer, tetramer and so on. Therefore, the reference of Lee teaches and had possession of the 'native tetrameric form' before running the SDS-PAGE denaturing gel to elucidate the nature of subunits or the tetrameric form of the native protein. Therefore, it is incorrect to say that the preparations of uricase obtained by Lee for use in the preparative or analytical SDS-PAGE disclosed in that reference are not in the native tetrameric form.

As may be noted most of the other arguments presented here are a repeat of previous arguments not relevant to the claims presented here. The claim language is changed but Applicants arguments do not address any specific reasons how the amended claim language would overcome the rejections. The claims as amended are

broader than claims previously presented and explained in the anticipation rejection, therefore do not overcome the rejection(s) presented here.

8. No claim is allowed.

9. Claims 54-59 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571) 272 0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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